

## WEST Search History

DATE: Thursday, September 12, 2002

Set Name Query  
side by side

Hit Count Set Name  
result set

*DB=USPT; PLUR=YES; OP=ADJ*

L8	L7 and theobromine	12	L8
L7	L6 and 7-methylxanthine	27	L7
L6	methylxanthine	724	L6
L5	l1 and transgenic	13	L5
L4	L3 and coffee	4	L4
L3	L2 and (gene or cdna or coding region)	189	L3
L2	L1 and caffeine	820	L2
L1	theobromine	1032	L1

END OF SEARCH HISTORY

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1649axm

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America  
NEWS 2 Apr 08 "Ask CAS" for self-help around the clock  
NEWS 3 Apr 09 BEILSTEIN: Reload and Implementation of a New Subject Area  
NEWS 4 Apr 09 ZDB will be removed from STN  
NEWS 5 Apr 19 US Patent Applications available in IFICDB, IFIPAT, and IFIUDB  
NEWS 6 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS  
NEWS 7 Apr 22 BIOSIS Gene Names now available in TOXCENTER  
NEWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available  
NEWS 9 Jun 03 New e-mail delivery for search results now available  
NEWS 10 Jun 10 MEDLINE Reload  
NEWS 11 Jun 10 PCTFULL has been reloaded  
NEWS 12 Jul 02 FOREGE no longer contains STANDARDS file segment  
NEWS 13 Jul 22 USAN to be reloaded July 28, 2002;  
saved answer sets no longer valid  
NEWS 14 Jul 29 Enhanced polymer searching in REGISTRY  
NEWS 15 Jul 30 NETFIRST to be removed from STN  
NEWS 16 Aug 08 CANCERLIT reload  
NEWS 17 Aug 08 PHARMAMarketLetter(PHARMAML) - new on STN  
NEWS 18 Aug 08 NTIS has been reloaded and enhanced  
NEWS 19 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)  
now available on STN  
NEWS 20 Aug 19 IFIPAT, IFICDB, and IFIUDB have been reloaded  
NEWS 21 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded  
NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced  
NEWS 23 Sep 03 JAPIO has been reloaded and enhanced  
  
NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,  
CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),  
AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002  
NEWS HOURS STN Operating Hours Plus Help Desk Availability  
NEWS INTER General Internet Information  
NEWS LOGIN Welcome Banner and News Items  
NEWS PHONE Direct Dial and Telecommunication Network Access to STN  
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 17:57:01 ON 12 SEP 2002

=> file agricola  
COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
0.21	0.21

FULL ESTIMATED COST

FILE 'AGRICOLA' ENTERED AT 17:57:49 ON 12 SEP 2002

FILE COVERS 1970 TO 11 Jul 2002 (20020711/ED)

Compiled and distributed by the National Agricultural Library  
of the Department of Agriculture of the United States of  
America. It contains copyrighted material. All rights  
reserved. (1996)

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

=> s coffee and transgenic

5910 COFFEE

10399 TRANSGENIC

L1 6 COFFEE AND TRANSGENIC

=> dup rem l1

PROCESSING COMPLETED FOR L1

L2 6 DUP REM L1 (0 DUPLICATES REMOVED)

=> d 1-6 ti

L2 ANSWER 1 OF 6 AGRICOLA

TI Cichorium intybus L--cultivation, processing, utility, value addition and  
biotechnology, with an emphasis on current status and future prospects.

L2 ANSWER 2 OF 6 AGRICOLA

TI In vivo modification of the cell wall polysaccharide galactomannan of guar  
transformed with alpha-galactosidase gene cloned from senna.

L2 ANSWER 3 OF 6 AGRICOLA

TI Genetically modified **coffee** plants expressing the Bacillus  
thuringiensis cry1Ac gene for resistance to leaf miner.

L2 ANSWER 4 OF 6 AGRICOLA

TI **Transgenic** plants of **coffee** Coffea canephora from  
embryogenic callus via Agrobacterium tumefaciens-mediated transformation.

L2 ANSWER 5 OF 6 AGRICOLA

TI Susceptibility of the **coffee** leaf miner (Perileucoptera spp.) to  
Bacillus thuringiensis delta-endotoxins: a model for **transgenic**  
perennial crops resistant to endocarpic insects.

L2 ANSWER 6 OF 6 AGRICOLA

TI Glufosinate as an efficient inhibitor of callus proliferation in  
**coffee** tissue.

=> d 3 so

L2 ANSWER 3 OF 6 AGRICOLA

SO Plant cell reports, Mar 2000. Vol. 19, No. 4. p. 382-389  
Publisher: Berlin : Springer-Verlag.  
CODEN: PCRPD8; ISSN: 0721-7714

=> d 6 ab

L2 ANSWER 6 OF 6 AGRICOLA

=> d 6 so

L2 ANSWER 6 OF 6 AGRICOLA

SO In vitro cellular & developmental biology. Plant : journal of the Tissue Culture Association, Jan/Mar 1997. Vol. 33, No. 1. p. 6-12  
Publisher: Columbia, MD : Society for In Vitro Biology.  
CODEN: IVCPEO; ISSN: 1054-5476

=> d 4 so

L2 ANSWER 4 OF 6 AGRICOLA

SO Plant cell reports, Dec 1999. Vol. 19, No. 2. p. 106-110  
Publisher: Berlin : Springer-Verlag.  
CODEN: PCRPD8; ISSN: 0721-7714

=> 3 ab

3 IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> d 3 ab

L2 ANSWER 3 OF 6 AGRICOLA

=> d 5 ab

L2 ANSWER 5 OF 6 AGRICOLA

AB Binding of several *Bacillus thuringiensis* delta-endotoxins was studied on histological midgut sections of larvae of **coffee** leaf miner *Perileucoptera coffeella* from Brazil and *Perileucoptera* sp from Madagascar. CryIA(a), CryIA(b), CryIA(c), CryIB, CryIE, and CryIIA were tested for binding, and only CryIA(c), CryIB, and CryIE yielded a positive response. The toxins bound to the whole midgut, and the result was identical on both insect populations. The same toxins, to the number of which CryIC was added, were tested on larvae of *P. coffeella*. CryIA(c) and CryIB were toxic with an LC50 of 1.47 micrograms/ml and 21.93 micrograms/ml, respectively. CryIE was not toxic to *P. coffeella*. CryIA(c) and CryIB were tested for synergistic activity and were shown to act by cumulative effect when delivered to the insect larvae as a mixture.

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:sssptal649axm

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2	Apr 08	"Ask CAS" for self-help around the clock
NEWS	3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS	4	Apr 09	ZDB will be removed from STN
NEWS	5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS	6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS	7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS	8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS	9	Jun 03	New e-mail delivery for search results now available
NEWS	10	Jun 10	MEDLINE Reload
NEWS	11	Jun 10	PCTFULL has been reloaded
NEWS	12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS	13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS	14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS	15	Jul 30	NETFIRST to be removed from STN
NEWS	16	Aug 08	CANCERLIT reload
NEWS	17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS	18	Aug 08	NTIS has been reloaded and enhanced
NEWS	19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS	20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS	21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS	22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS	23	Sep 03	JAPIO has been reloaded and enhanced
NEWS EXPRESS			February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS			STN Operating Hours Plus Help Desk Availability
NEWS INTER			General Internet Information
NEWS LOGIN			Welcome Banner and News Items
NEWS PHONE			Direct Dial and Telecommunication Network Access to STN
NEWS WWW			CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 09:36:04 ON 12 SEP 2002

=> file agricola caplus biosis  
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.21	0.21

FULL ESTIMATED COST

FILE 'AGRICOLA' ENTERED AT 09:36:24 ON 12 SEP 2002

FILE 'CAPLUS' ENTERED AT 09:36:24 ON 12 SEP 2002  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 09:36:24 ON 12 SEP 2002  
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

=> s theobromine  
L1 4234 THEOBROMINE

=> s l1 and (gene or cdna or coding region)  
L2 36 L1 AND (GENE OR CDNA OR CODING REGION)

=> dup rem l2  
PROCESSING COMPLETED FOR L2  
L3 29 DUP REM L2 (7 DUPLICATES REMOVED)

=> d 1-10 ti

L3 ANSWER 1 OF 29 CAPLUS COPYRIGHT 2002 ACS  
TI **cdna** and protein sequences of Coffea arabica **theobromine**  
synthase isoforms and their used for caffeine biosynthesis

L3 ANSWER 2 OF 29 CAPLUS COPYRIGHT 2002 ACS  
TI **cdna** and protein sequences of coffee and tea N-methyltransferase  
and their uses for caffeine synthesis

L3 ANSWER 3 OF 29 CAPLUS COPYRIGHT 2002 ACS  
TI Modulation of histone deacetylase, drug screening method, and treatment  
methods

L3 ANSWER 4 OF 29 CAPLUS COPYRIGHT 2002 ACS  
TI Leptin for use in inhibition of endothelial cell proliferation optionally  
together with VEGF inhibitors

L3 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2002 ACS  
TI Methods for treating immunomediated inflammatory disorders and changing  
skin pigmentation

L3 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2002 ACS  
TI Treatment and prevention of hepatic disorders with vitamin E,  
pentoxifylline compounds, and 2,6-di-tert-butylphenol derivatives

L3 ANSWER 7 OF 29 CAPLUS COPYRIGHT 2002 ACS  
TI Treatment of narcolepsy and isolated cataplexy with immunosuppressants

L3 ANSWER 8 OF 29 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1  
TI 7-methylxanthine methyltransferase of coffee plants. **Gene**  
isolation and enzymatic properties

L3 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2002 ACS  
TI **cdna** cloning of caffeine (**theobromine**) synthase from  
coffee (Coffea arabica L.)

L3 ANSWER 10 OF 29 CAPLUS COPYRIGHT 2002 ACS  
TI Protein and cDNA sequences of a novel Camellia sinensis  
N-methyltransferase involved in caffeine biosynthesis and uses thereof

=> d ab

L3 ANSWER 1 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AB This invention provides cDNA and protein sequences of four  
theobromine synthases cloned from Coffea arabica. The enzymes  
catalysis of the theobromine synthesis from 7-Me xanthine. The  
sequence of these enzymes can be used for prepn. of transgenic plant for  
increase the caffeine content or produce caffeine less coffee by knocking  
repression the expression of the gene.

=> d pi

L3	ANSWER 1 OF 29	CAPLUS	COPYRIGHT 2002 ACS		
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2002112785	A2	20020416	JP 2000-307149	20001006
	EP 1197558	A2	20020417	EP 2001-122628	20010927
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 2002108143	A1	20020808	US 2001-971020	20011005

=> d 2 ab

L3 ANSWER 2 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AB The invention provides the cDNA and protein sequences of coffee  
and tea N-Me transferase as well as the consensus sequence of them. The  
enzyme also has catalytic activity of 7-methylxanthine  
N-3-methyltransferase, theobromine N-1-methyltransferase and  
paraxanthine N-3-methyltransferase. The sequences can be used for  
caffeine biosynthesis in transgenic plants.

=> d 2 pi

L3	ANSWER 2 OF 29	CAPLUS	COPYRIGHT 2002 ACS		
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2002085072	A2	20020326	JP 2000-275063	20000911

=> d 8 ab

L3 ANSWER 8 OF 29 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1  
AB Caffeine is synthesized through sequential three-step methylation of  
xanthine derivs. at positions 7-N, 3-N, and 1-N. However, controversy  
exists as to the no. and properties of the methyltransferases involved.  
Using primers designed on the basis of conserved amino acid regions of tea  
caffeine synthase and Arabidopsis hypothetical proteins, a particular DNA  
fragment was amplified from an mRNA population of coffee plants.  
Subsequently, this fragment was used as a probe, and four independent  
clones were isolated from a cDNA library derived from coffee  
young leaves. Upon expression in Escherichia coli, one of them was found  
to encode a protein possessing 7-methylxanthine methyltransferase activity  
and was designated as CaMXMT. It consists of 378 amino acids with a  
relative mol. mass of 42.7 kDa and shows similarity to tea caffeine  
synthase (35.8%) and salicylic acid methyltransferase (34.1%). The  
bacterially expressed protein exhibited an optimal pH for activity ranging

between 7 and 9 and methylated almost exclusively 7-methylxanthine with low activity toward paraxanthine, indicating a strict substrate specificity regarding the 3-N position of the purine ring. Km values were estd. to be 50 and 12  $\mu$ M for 7-methylxanthine and S-adenosyl-L-methionine, resp. Transcripts of CaMXMT could be shown to accumulate in young leaves and stems contg. buds, and green fluorescent protein fusion protein assays indicated localization in cytoplasmic fractions. The results suggest that, in coffee plants, caffeine is synthesized through three independent methylation steps from xanthosine, in which CaMXMT catalyzes the second step to produce **theobromine**.

=> d 8 so

L3 ANSWER 8 OF 29 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1  
S0 Journal of Biological Chemistry (2001), 276(11), 8213-8218  
CODEN: JBCHA3; ISSN: 0021-9258

=> d 9 ab

L3 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AB Caffeine synthase (CS), the S-adenosylmethionine (SAM)-dependent N-methyltransferase is a key enzyme for caffeine biosynthesis, since this enzyme is involved in the last two-methylation steps. The CS protein was purified from young tea leaves and subsequently the CS **cdna**, named TCS, was isolated (Kato et al., 2000). To isolate **cdna** clones encoding CS from coffee, we established a **cdna** library from young coffee leaves and carried out screening of this. Oligonucleotides corresponding to the consensus sequences, which form the putative SAM binding region of TCS, were synthesized and used for RT-PCR as primers. The resulting PCR products were used to screen approx. 5.0.times.10<sup>5</sup> plaques from a coffee **cdna** library. Finally, independent five **cdna** clones, termed CCS clones, were isolated and analyzed those sequences. The predicted amino acid sequences of the CCS clones are over 80% identical among those of the clones and share almost 40% identity with those of TCS and salicylic acid carboxyl methyltransferase from *Clarkia breweri*, resp. The mol. masses of these proteins were almost the same (approx. 43 kDa). These values agree well with that of TCS protein (41 kDa). We have established expression systems of CCS cDNAs in *E. coli*. Some transformants have produced recombinant proteins. **Theobromine** producing activity was confirmed in some kinds of recombinant proteins.

=> d 9 so

L3 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2002 ACS  
S0 Colloque Scientifique International sur le Cafe (2001), 19th, 815-818  
CODEN: CICRD8

=> d 10 ab

L3 ANSWER 10 OF 29 CAPLUS COPYRIGHT 2002 ACS  
AB The present invention provides protein and **cdna** sequences of a novel *Camellia sinensis* N-methyltransferase, one of the enzymes constituting a caffeine biosynthesis system, which simultaneously have activities of three Me transferases, 7-Me xanthine N3 Me transferase, **theobromine** N1 Me transferase and paraxanthine N3 Me transferase. Thanks to the present invention, N-Me transferase that can be utilized as an industrial, food, or medical enzyme, can be produced efficiently. The present invention makes it possible to modify caffeine biosynthesis metab. of caffeine productive plants, plant tissues, or plant cells, for



efficiently producing caffeine metab. based compds. Furthermore, the caffeine biosynthesis metab. of caffeine productive plants, plant tissues, or plant cells can be modified, thereby modifying the prodn. rate of a caffeine metab. based compd. group.

=> d 10 pi

L3	ANSWER 10 OF 29 CAPLUS COPYRIGHT 2002 ACS				
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	-----	-----	-----	-----
PI	EP 1055727	A2	20001129	EP 2000-304522	20000526
	EP 1055727	A3	20010919		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
	IE, SI, LT, LV, FI, RO				
	JP 2001037490	A2	20010213	JP 2000-151718	20000523

=> d 11-20 ti

L3	ANSWER 11 OF 29 CAPLUS COPYRIGHT 2002 ACS	
TI	Properties of CFTR activated by the xanthine derivative X-33 in human airway Calu-3 cells	
L3	ANSWER 12 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.	
TI	Can caffeine metabolism be used as an in-vivo probe for human flavin-containing monooxygenase activity.	
L3	ANSWER 13 OF 29 CAPLUS COPYRIGHT 2002 ACS	
TI	The stimulatory action and the development of tolerance to caffeine is associated with alterations in <b>gene</b> expression in specific brain regions	
L3	ANSWER 14 OF 29 CAPLUS COPYRIGHT 2002 ACS	DUPLICATE 2
TI	Flavin monooxygenase 3 (FMO3) polymorphism in a white population: allele frequencies, mutation linkage, and functional effects on clozapine and caffeine metabolism	
L3	ANSWER 15 OF 29 CAPLUS COPYRIGHT 2002 ACS	DUPLICATE 3
TI	Phenotyping of flavin-containing monooxygenase using caffeine metabolism and genotyping of FMO3 <b>gene</b> in a Korean population	
L3	ANSWER 16 OF 29 CAPLUS COPYRIGHT 2002 ACS	
TI	Amine-substituted xanthinyl compounds, their preparation, and use for treatment of diseases caused by an undesirable cell response mediated by a proliferative intracellular signaling pathway	
L3	ANSWER 17 OF 29 CAPLUS COPYRIGHT 2002 ACS	
TI	Human immunodeficiency virus type 1 vpr <b>gene</b> induces phenotypic effects similar to those of the DNA alkylating agent, nitrogen mustard	
L3	ANSWER 18 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.	
TI	Intoxication with dextromethorphan in an adolescent with a genetic cytochrome P450 CYP2D6 deficiency.	
L3	ANSWER 19 OF 29 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.	
TI	Effect of colchicine and methylated purines on nitrous acid-induced <b>gene</b> conversion in <i>Saccharomyces cerevisiae</i> .	
L3	ANSWER 20 OF 29 CAPLUS COPYRIGHT 2002 ACS	
TI	Continuous microbial manufacture of xanthines	

=> d 13 ab

L3 ANSWER 13 OF 29 CAPLUS COPYRIGHT 2002 ACS  
 AB The authors sought neurochem. correlates to the stimulatory action of caffeine in rats and to adaptations during development of tolerance. Acute i.p. injections of caffeine (7.5 mg/kg) increased locomotion and NGFI-A mRNA, a marker of neuronal activity, in the hippocampal area CA1, but decreased NGFI-A mRNA in rostral striatum and nucleus accumbens. Rats that received caffeine (0.3 gm/L) in their drinking water for 14 d developed tolerance to the stimulatory effect of a challenge with caffeine (7.5 mg/kg) and responded with a less pronounced decrease of NGFI-A mRNA in rostral striatum and nucleus accumbens. Metab. of caffeine to its active metabolites was increased in tolerant animals, but the total level of active metabolites in brain was not significantly altered. Thus, there are changes in caffeine metab. after long-term caffeine treatment, but they cannot explain development of tolerance. Caffeine-tolerant animals had downregulated levels of adenosine A2A receptors and the corresponding mRNA in rostral parts of striatum, but an increased expression of adenosine A1 receptor mRNA in the lateral amygdala. No changes in mesencephalic tyrosine hydroxylase mRNA were found in caffeine-tolerant rats. Thus, the authors have identified neuronal pathways that are regulated by adenosine A1 and/or A2A receptors and are targets for the stimulatory action of caffeine. Furthermore, adaptive changes in gene expression in these brain areas were assocd. with the development of locomotor tolerance to caffeine.

=> d 21-29 ti

L3 ANSWER 21 OF 29 CAPLUS COPYRIGHT 2002 ACS  
 TI Effect of different xanthines and phosphodiesterase inhibitors on c-fos expression in rat striatum

L3 ANSWER 22 OF 29 CAPLUS COPYRIGHT 2002 ACS  
 TI A binding site model and structure-activity relationships for the rat A3 adenosine receptor

L3 ANSWER 23 OF 29 CAPLUS COPYRIGHT 2002 ACS  
 TI Caffeine metabolism in a healthy Spanish population: N-acetylator phenotype and oxidation pathways

L3 ANSWER 24 OF 29 CAPLUS COPYRIGHT 2002 ACS  
 TI The performance of short-term tests in identifying potential germ cell mutagens: a qualitative and quantitative analysis

L3 ANSWER 25 OF 29 CAPLUS COPYRIGHT 2002 ACS  
 TI A caffeine demethylase gene from Pseudomonas and its use in the microbial manufacture of 3-methyl-7-alkylxanthines

L3 ANSWER 26 OF 29 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4  
 TI Caffeine, estradiol, and progesterone interact with human CYP1A1 and CYP1A2. Evidence from cDNA-directed expression in Saccharomyces cerevisiae

L3 ANSWER 27 OF 29 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 5  
 TI Caffeine as a probe for human cytochromes P450: validation using cDNA-expression, immunoinhibition and microsomal kinetic and inhibitor techniques

L3 ANSWER 28 OF 29 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6  
 TI Biotransformation of caffeine, paraxanthine, theobromine, and theophylline by cDNA-expressed human CYP1A2 and CYP2E1

L3 ANSWER 29 OF 29 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 7  
 TI Effect of colchicine and methylated purines on UV-induced mitotic

gene conversion in *Saccharomyces cerevisiae*

=> d 28 ab

L3 ANSWER 28 OF 29 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6  
AB Six human cytochrome P450s expressed in HepG2 cells using vaccinia virus cDNA-directed expression, were used to study the biotransformation of caffeine and its metabolites. CYP1A2 alone was responsible for caffeine 3-demethylation and paraxanthine 7-demethylation; in addn., 1A2 catalyzed virtually all reactions related to caffeine and its metabolites. The metabolic profile of caffeine biotransformation by CYP1A2 averaged 81.5% for paraxanthine, 10.8% for **theobromine** and 5.4% for theophylline formation. It remained quite uniform when caffeine concns. were varied. The most striking finding was that CYP2E1 (the ethanol-inducible form) had major influences upon caffeine metab.: in particular, it catalyzed the formation of theophylline and **theobromine** from caffeine. Thus, the in vivo metabolite profiling of caffeine may reveal CYP2E1 activities in addn. to the previously documented activities of CYP1A2, polymorphic N-acetyltransferase and xanthine oxidase.

=> s 11 and transgenic

L4 3 L1 AND TRANSGENIC

=> dup rem l4

PROCESSING COMPLETED FOR L4

L5 3 DUP REM L4 (0 DUPLICATES REMOVED)

=> d 1-3 ti

L5 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS  
TI cDNA and protein sequences of *Coffea arabica* **theobromine** synthase isoforms and their used for caffeine biosynthesis

L5 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS  
TI cDNA and protein sequences of coffee and tea N-methyltransferase and their uses for caffeine synthesis

L5 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS  
TI Biosynthesis and metabolism of caffeine and related purine alkaloids in plants

=> d 3 ab

L5 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS  
AB A review with many refs. Caffeine and other purine alkaloids, including **theobromine** and theophylline, have played a major role in the long-standing popularity of non-alc. beverages and foods such as coffee, tea, cocoa, mate, chocolate and a wide range of soft drinks. Nearly 100 plant species have been identified as contg. these purine alkaloids; the more common are from the genera *Camellia*, *Coffea*, *Cola*, *Ilex*; *Paullinia* and *Theobroma*. [Equation Omitted]. This review begins by summarizing those aspects of general purine metab. in plants that are related to purine alkaloid metab., and then provides an up-to-date account of the biosynthesis of caffeine and **theobromine** in a variety of plant species. Recent information on the properties and isolation of key enzymes, such as the caffeine synthase, are presented. Physiol. studies on caffeine biosynthesis in tea and coffee plants including the authors' own work are also introduced. Catabolism of caffeine via demethylation to xanthine and degrdn. via the purine catabolism pathway in higher plants is then reviewed. The diversity of caffeine catabolism between species and

between tissues of different age is considered. In young tea leaves, theophylline, a catabolite of caffeine, is reutilized for caffeine synthesis, but in aged *Coffea arabica* leaves 7-methylxanthine accumulates. Some *Coffea* species convert caffeine to methyluric acids. Finally, biotechnol. of purine alkaloids including caffeine prodn. in tissue and cell cultures and the possibilities of producing decaffeinated beverages through the use of **transgenic** coffee and tea plants are described. (c) 1999 Academic Press.

=> d 3 so

L5 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS  
 SO Advances in Botanical Research (1999), 30, 117-205  
 CODEN: ABTRAJ; ISSN: 0065-2296

=> s 7 methlyxanthine  
 L6 0 7 METHLYXANTHINE

=> s methylxanthine  
 L7 7452 METHYLXANTHINE

=> s 17 and coffee  
 L8 200 L7 AND COFFEE

=> s 18 and theobromine  
 L9 84 L8 AND THEOBROMINE

=> s 19 and (gene or cdna or coding regon)  
 L10 4 L9 AND (GENE OR CDNA OR CODING REGON)

=> dup rem l10  
 PROCESSING COMPLETED FOR L10  
 L11 3 DUP REM L10 (1 DUPLICATE REMOVED)

=> d 1-3 ti

L11 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS  
 TI **cdna** and protein sequences of *Coffea arabica* **theobromine**  
 synthase isoforms and their used for caffeine biosynthesis

L11 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS  
 TI **cdna** and protein sequences of **coffee** and tea  
 N-methyltransferase and their uses for caffeine synthesis

L11 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1  
 TI 7-**methylxanthine** methyltransferase of **coffee** plants.  
**Gene** isolation and enzymatic properties

=> d 3 ab

L11 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1  
 AB Caffeine is synthesized through sequential three-step methylation of xanthine derivs. at positions 7-N, 3-N, and 1-N. However, controversy exists as to the no. and properties of the methyltransferases involved. Using primers designed on the basis of conserved amino acid regions of tea caffeine synthase and Arabidopsis hypothetical proteins, a particular DNA fragment was amplified from an mRNA population of **coffee** plants. Subsequently, this fragment was used as a probe, and four independent clones were isolated from a **cdna** library derived from **coffee** young leaves. Upon expression in *Escherichia coli*, one of them was found to encode a protein possessing 7-**methylxanthine**

methyltransferase activity and was designated as CaMXMT. It consists of 378 amino acids with a relative mol. mass of 42.7 kDa and shows similarity to tea caffeine synthase (35.8%) and salicylic acid methyltransferase (34.1%). The bacterially expressed protein exhibited an optimal pH for activity ranging between 7 and 9 and methylated almost exclusively 7-methylxanthine with low activity toward paraxanthine, indicating a strict substrate specificity regarding the 3-N position of the purine ring. Km values were estd. to be 50 and 12  $\mu$ M for 7-methylxanthine and S-adenosyl-L-methionine, resp. Transcripts of CaMXMT could be shown to accumulate in young leaves and stems contg. buds, and green fluorescent protein fusion protein assays indicated localization in cytoplasmic fractions. The results suggest that, in coffee plants, caffeine is synthesized through three independent methylation steps from xanthosine, in which CaMXMT catalyzes the second step to produce theobromine.

=> d 3 so

L11 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1  
SO Journal of Biological Chemistry (2001), 276(11), 8213-8218  
CODEN: JBCHA3; ISSN: 0021-9258